Developments in the treatment and diagnosis of anxiety disorders.

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A wide range of epidemiological community studies worldwide converge on several incontrovertible facts regarding anxiety disorders: they occur frequently, begin at an early age, significantly impair multiple areas of development and life, and are associated with numerous adverse correlates and consequences. Furthermore, evidence clearly points to the fact that the majority of patients who have anxiety disorders still go undetected and undertreated, despite considerable efforts over the last two decades to improve this situation.[1] Less than half receive any treatment at all and only a fraction of those receive what can be considered even "minimally adequate treatment."[2,3]

In addition to personal hardship resulting from anxiety disorders, increasing convergent evidence clearly points to an immense societal burden. Factors such as school failure, unemployment and underemployment, academic underachievement, interactional and marital problems, and excessive use of health care facilities insidiously combine so that the overall costs and burden to society are immense, with estimates of approximately $42 billion per year in the United States[4] and comparable rates in Europe.[2,5] Above and beyond monetary estimates, the costs extend outward from the patient and affect family and friends,[6] and multiple sources of evidence suggest that these costs are passed on to the next generation via an increased risk for mental health complications.[7,8]

Research over the past two decades ranging from cross-sectional and longitudinal epidemiological studies to clinical trials consistently documents the fact that mental disorders seldom occur in isolation.[2,9,10–13] Recent studies have contributed to a better understanding of the high rates of comorbidity, its implications, and, in some cases, the putative causes. Substantially increased rates of depressive disorders and, to a lesser degree, substance use disorders predominantly develop in the years after the onset of an anxiety disorder[14] (see article by Beesdo, Knappe, & Pine, in this issue). This has led many researchers to consider anxiety disorders as powerful—in fact, the

most powerful—risk factor for depression.[15–18] Further evidence of this assumption lies in the fact that there is a dose–response relationship between anxiety disorders and subsequent mental disorders and that different anxiety disorders carry substantially different risks.[17,18]

Nevertheless, after many years of investigation, it remains unclear which mechanisms and processes best account for the high comorbidity risk in the anxiety disorders. Some suggest direct and indirect pathways of anxiety–associated features and complications, such as neurobiological factors or persistent avoidance that in themselves contribute to anxiety patients' increased risk for depression.[15] Besides shared vulnerability factors (see articles by Beesdo, Knappe, & Pine, and by Martin, Ressler, Binder, & Nemeroff, both in this issue), likely candidates that have been considered are cognitive-behavioral factors (Arch & Craske, this issue) and neurobiological sensitization processes (Martin, Ressler, Binder, & Nemeroff, this issue), leading to an accumulation of depression-specific risk factors. Others have suggested that the high rates of comorbidity indicate the existence of an underlying shared higher-order factor or liability dimension for a range of anxiety and depressive and even somatoform disorders.[19–21] These explorations argue that all these disorders should be regarded as "internalizing" disorders, characterized by emotional dysregulation and a similar and only gradually different set of vulnerability and risk factors. This latter perspective has recently received considerable, yet controversial,[22] attention within the current revision process of DSM-V and ICD-11 (see article by Wittchen, Beesdo, & Gloster, this issue).[21–25] The allure of this model for some may be its implicit (but untested) promise of a seemingly simpler diagnostic classification system.

This special issue on anxiety disorders comes together at a time of much development in the understanding, treatment, and diagnosis of anxiety disorders and particularly the revision processes of DSM-V and ICD-11, both expected to come into effect in 2012. We therefore decided not only to invite our colleagues to review the latest evidence in their respective fields, but also to comment on and share their thoughts with regard to the need of changes in our future diagnostic classification manual.

The reader will notice a particular emphasis on cognitive-behavioral treatments (CBT) relative to psychopharmacology in this special issue. This is due to several factors. First, although some new substances for some anxiety disorders have been marketed since the last time this journal reviewed the field of anxiety disorders (December 1995; Vol. 18, No. 4) and despite the existence of some new compounds and treatment principles in development (Martin, Ressler, Binder, & Nemeroff, this issue), there is currently little news about pharmacological approaches that are likely to affect practice in the next few years. Thus, the diagnostic specific articles in this issue (McHugh, Smits, & Otto; Allgulander; Hoyer & Gloster; Jørstad-Stein & Heimberg; Hamm; Shalev; and Stein, Denys, Gloster, Holander, Leckman, Rauch, & Phillips) highlight primarily the evidence for efficacy of established pharmacological approaches in short- and long-term outcomes as well as combination treatments with some form of CBT.

Second, relative to pharmacology, CBT is widely misunderstood, in part due to the definitions—or lack thereof—used to describe the techniques, processes, and strategies implemented by CBT practitioners and the mental health field in general. As CBT has grown to become the treatment of choice for various disorders and all anxiety disorders in particular, it is increasingly unlikely that the interventions used by practitioners are consistent with state-of-the-art CBT and many others may even run counter to the principles underlying CBT. This state of affairs is no wonder given the fact that "CBT" has become a catch-all phrase to describe nearly anything and seems to have replaced the word psychotherapy in some circles. Further, some practitioners

not specifically trained in this modality nevertheless claim to deliver such treatments, motivated presumably by the desire to meet reimbursement requirements. Further complicating matters is that, unlike psychotropic medication, CBT's development and prescription are not strictly regulated. Thus, by focusing on CBT we hope to sensitize the practitioner to the fact that CBT as currently practiced might have little to do with CBT as derived from stringent research, or CBT as tested in randomized clinical trials.

Equally important, researchers also lack a clear understanding of the active and necessary treatment ingredients of what constitutes CBT. This is a core problem of the current CBT research field and represents a challenge for future research. Precise definitions are a prerequisite for any such attempt. What are the specific "cognitive" elements; what are the specific "behavioral" elements? What is their specific effect on dysfunctions of the "fear circuitry" in the brain and associated neurobiologic variables.[26,27] What therapeutic elements do unspecific elements constitute in relation to unspecific general factors of improvements, and which elements are unique? Is exposure in vivo a CBT variant? Which elements are unique for one versus another disorder? How does CBT in social phobia differ from CBT in PTSD and GAD? These are just a few examples of core research questions that need to be resolved if CBT wants to maintain the original claim that the method is scientifically sound and based on proper research. Only after this is established can mental health practitioners accurately examine their own skills to determine whether they posses the competences necessary to optimally treat the individual anxiety disorders.

The time has come to challenge the idea that CBT is simply a group of heterogeneous interventions, with the only prerequisite to be considered "CBT" is that they be loosely tied to a cognitive or behavioral conceptual model or be part of an empirically supported treatment *package*. Instead, a new generation of research needs to be initiated that investigates the modes, processes, and mechanisms of therapeutic action. This is the reason why we emphasized the use of precise definitions throughout the articles. When an accurate understanding of the active treatment ingredients is combined with an accurate self-assessment from the practitioner of his/her competencies in these mechanisms, the entire field is in a much stronger position to harness the knowledge of our state-of-the-art treatments, closely tied to basic science investigations, and in the service of our patients.

Third, we wanted to identify those components of CBT treatments that are currently believed to be active ingredients, even if the mechanisms through which they work are unclear. The reader will clearly notice that several interventions are common across disorders, both for pharmacological and psychological approaches. These include SSRI medication and, as evident in this special issue, various components of CBT such as exposure, emotional engagement, and techniques targeting reevaluation of thoughts. Indeed, research has begun to address the commonality of the disorders via treatment protocols[28,29] and explicit discussion of psychological processes extending from classical and operant conditioning and associated techniques.[30–32]

Techniques, in turn, are sometime more and sometimes less derived from basic scientific principles. Certain individual principles and techniques derived from these *do* cut across diagnoses. Chief among these are basic science principles of classical and operant conditioning and the techniques derived from them (ie, exposure, diffusion, etc.). The very nature of treatment validation, however, has limited our ability to indicate precisely which techniques and strategic maneuvers based on which exact scientific principles are at play. Therefore, identification of such dimensions vary depending on one's perspective, a troubling fact in itself. A partial list of potential dimensions ranges from learning theory (avoidance, reinforcement, fusion, etc.) to

clinical cognitive theory (schemas, maladaptive cognitions, etc.), to experimental psychopathology (eg, attention biases), to emotional theory (antecedent and consequential control) to psychodynamic concepts (eg, repression, defense mechanism, etc.). In the next few years, the field must work towards a better understanding of which dimensions are the direct causal agents involved in therapeutic improvement and which are simply byproducts.

A fourth reason for the relative concentration on CBT in this issue surrounds the exciting developments that have occurred across the spectrum of anxiety disorders. Acceptance and Commitment Therapy (ACT) is one example of these developments, as is evident in most disorder-specific chapters in this issue. ACT can be seen as an example of a therapeutic stance that tries to develop interventions in close coordination with basic science. The evidence for its efficacy in anxiety disorders to date is preliminary, promising, and growing. In part, these and other similar developments arose in response to the recognition that superficial definitions of CBT and its requisite components would not lead to optimized outcomes.

Finally, we wish to acknowledge something that is seldom discussed in science, namely our own bias. In this case, our bias towards psychological treatments—in particular, variations of CBT—in our daily practice and research make us more keenly aware of the critical and crucial elements involved in this form of treatment.

Some readers might note a number of important topics that are missing, for example a chapter on translational research and service provision or on prevention. Certainly there is a range of remarkable and promising developments in the field that would have deserved close scrutiny, which were, however, impossible to cover because of page restrictions, although they were addressed to some degree in most disorder-specific chapters.

Nevertheless, we wish to emphasize the paradox that effective treatments are available, yet they reach only a minority of people affected. This situation remains a core concern that is evidently specific to many anxiety disorders. It differs from depression, where increasing treatment rates have been monitored. The paradox that CBT, the preferred method for many anxiety disorders, is still not widely available signals the need for further, more targeted action. We believe it is unlikely that recent attempts to make CBT shorter and simpler or to make it available by electronic media and telephone[33] so that it can be delivered by all health care professions or, in its extreme, without them will in and of themselves be an adequate solution. Unless we better understand how, why, and when CBT is effective in which disorder and with what type of patients, such demonstrations are not likely to be promising and might in fact lead to a corruption of CBT's scientific base and a devaluation of this method as a whole. Thus, we hope to stimulate a rethinking of the term CBT and a reorientation to its scientific foundations with the goal of specification and improvement.

Similar concerns can be expressed with regard to prevention. The moderately (and sometimes counterintuitive) negative effects of group-based general preventive efforts—frequently based on CBT methods—as compared with targeted high-risk approaches suggest that we need to better understand pathogenic pathways.[34,35] We believe that the uncritical group-based preventive strategies, typically showing limited efficacy in the field, suffer from a lack in anxiety-specific concepts about the core etiological pathways associated with the various anxiety disorders. Unless these pathways are better understood, it seems unlikely that we will ultimately be able to present more convergent and persuasive evidence on the efficacy of CBT.

We hope that this special issue offers guidance to the practitioners, aids in training (especially in light of the APA regulations regarding training of CBT), stimulates research, and leads to discussions between all those involved in the treatment of

patients who have anxiety disorders. The field has progressed a long way in the last several decades. We hope and trust that the some of the critical reflections found within the pages of this special issue contribute to the refinement of this mission.

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